toleragenic properties of the claimed conjugate allow the practitioner to prepare the test animal for use in experimental methods that require repeated inoculation of the animal with the parental antibody fragment. It is noted that the conjugates can be successfully used for tolerization even if it assumed that conformational perturbations take place, since conformational perturbation will not alter linear epitopes. Moreover, tolerization with conformationally perturbed antibody conjugates would also provide valuable information to a researcher interested in identifying those portions of an antibody fragment that do not contribute to conformational epitopes recognized as foreign antigens in a particular animal model. Such information would be useful in the development of a deantigenized antibody fragment in a particular animal model.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Attached hereto is a marked-up version of the changes made to claim 1 by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Applicants respectfully request that a timely Notice of Allowance be issues in this case.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: May 24, 2002

By: _____

Ginger R. Dreger
Registration No. 33,055
Attorney of Record
620 Newport Center Drive
Sixteenth Floor
Newport Beach, CA 92660
(415) 954-4114

Version with markings to show changes made

Claim 1 has been amended as follows:

1. (Three-times amended) A conjugate consisting essentially of at least one antibody fragment covalently attached to no more than about 2 nonproteinaceous polymer molecules, wherein the apparent size of the conjugate is at least about 500 kD, wherein the antibody fragment comprises a heavy chain and a light chain corresponding to a heavy chain and a light chain portion of a parental antibody, wherein said heavy chain portion is free of the heavy chain constant domains of the Fc region, and wherein in the portion of the parental antibody the heavy and light chains are covalently linked by a disulfide bond between a cysteine residue in the light chain and a cysteine residue in the heavy chain, wherein in the antibody fragment the cysteine residue in the light or heavy chain is substituted with another amino acid and the cysteine residue in the opposite chain is covalently linked to a nonproteinaceous polymer molecule, and wherein at least one antibody fragment comprises an antigen binding site [that binds to] <u>for</u> a polypeptide selected from the group consisting of: human vascular endothelial growth factor (VEGF), human p185 receptor-like tyrosine kinase (HER2), human CD20, human CD18, human CD11a, human IgE, human Apo-2 receptor, human tumor necrosis factor-α (TNF-α), human tissue factor (TF), human α4β7 integrin, human GPIIb-IIIa integrin, human epidermal growth factor receptor (EGFR), human CD3, and human interleukin-2 receptor α-chain (TAC).